

Appl. Ser. No. 10/617, 573  
Art Unit 1646

Response and Amendment under § 1.111

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AMENDMENTS

In the Title:

Please amend the title of the application to read as follows: "Pharmaceutical Compositions, Kits, and Therapeutic Uses of Antagonist Antibodies to IL-17E."

In the Specification:

In the specification, please delete the paragraph entitled "Related Applications" beginning at page 1, line 2 as added by the Preliminary Amendment dated July 11, 2003 and add the following new paragraph beginning at page 1, line 2:

This application is a continuation of US application 10/000,157, filed Oct. 20, 2001; which is a continuation-in-part of US application 09/931,836, filed Aug. 16, 2001; which is a continuation-in-part of 09/929,404, filed Aug. 13, 2001; which is a continuation-in-part of US application 09/918,585, filed Jul. 30, 2001; which is a continuation-in-part of US application 09/908,827, filed Jul. 18, 2001; which is a continuation-in-part of US application 09/747,259, filed Dec. 20, 2000; which claims priority from provisional application 60/175,481, filed Jan. 11, 2000; and where US application 09/908,827 is a continuation-in-part of PCT/US01/21735, filed Jul. 9, 2001; which is a continuation-in-part of PCT/US01/21066, filed Jun. 29, 2001; which is a continuation-in-part of PCT/US01/19692, filed Jun. 20, 2001; which is a continuation-in-part of 09/874,503, filed Jun. 5, 2001; which is a continuation-in-part of PCT/US01/17800, filed Jun. 1, 2001; which is a continuation-in-part of both US application 09/854,280 and US application 09/854,208, both of which were filed May 10, 2001; which are both continuations-in-part of US application 09/816,744, filed Mar. 22, 2001; which is a continuation-in-part of PCT/US01/06520, filed Feb. 28, 2001; which is a continuation-in-part of both PCT/US00/34956, and US application 09/747,259, both filed Dec. 20, 2000; which are both continuations-in-part of PCT/US00/30873, filed Nov. 10, 2000; which is a continuation-in-part of PCT/US00/23328, filed Aug. 24, 2000.

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In the specification, please amend the paragraph on page 26, line 15 to line 21 as follows:

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acid Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from the National Center for Biotechnology Information's website <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National ~~Institute~~ Institutes of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

Also in the specification, please amend the paragraph on page 28, line 36 to page 29, line 5 as follows:

Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acid Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from the National Center for Biotechnology Information's website <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National ~~Institute~~ Institutes of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

Also in the specification, please amend the paragraph on page 22, lines 20-22 as follows:

Figure 59 demonstrates the up-regulation of IL-17E receptor (mIL-17ER) expression in mouse IL-17E transgenics versus non-transgenics as determined by Taqman TAQMAN<sup>TM</sup> analysis

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(PCR analysis technique for measuring gene expression using *Thermus aquaticus* DNA polymerase) (Perkin Elmer) in lung, kidney, liver, spleen and heart tissue.

Also in the specification, please amend the paragraph on page 128, lines 23-30 as follows:

B. Western Blot, Northern Blot and ~~Taqman~~<sup>TM</sup> TAQMAN<sup>TM</sup> Analysis:

Western blot analysis of binding of IL-17E (PRO10272) to IL-17RH1 (PRO5801) was performed essentially as described by Xie *et al.*, Cytokine, **11**(10): 729-735 (1999) and Xie *et al.*, J. Biol. Chem., **275**(40): 31335-31339 (2000). For Northern blot analysis, multiple tissue Northern blots (Clontech) were probed with a <sup>32</sup>P-labeled probe of random primed IL-17RH1 cDNA according to manufacturer's recommendations and exposed to X-omat (Kodak) for 72 hours. For quantitative PCR analysis (~~Taqman~~<sup>TM</sup> TAQMAN<sup>TM</sup>) total mRNA from human tissues (50 ng) was analyzed as recommended (Perkin Elmer) with primers based on the coding sequence of IL-17RH1.

Also in the specification, please amend the paragraph on page 151, lines 1-18 as follows:

A. Materials and Methods

*Generation of mIL-17E transgenic mice*

The cDNA encoding for the mature murine IL-17E protein (herein designated SEQ ID NO:41) with the putative signal sequence from human IL-17E (PRO10272; SEQ ID NO:6) was cloned into a plasmid containing rat myosin light chain promoter sequence followed by a sequence derived from the human growth hormone gene (hGH) including the 4<sup>th</sup> and 5<sup>th</sup> exons and 3' UTR plus poly A to improve expression of the transgene (see Faerman, A., and Shani, M., Development **118**:919 (1993); and Shani, M. et al., Mol. Cell. Biol. **8**:1006 (1998). The expression cassette fragment was excised and purified and injected into one-cell mouse eggs prepared from FVBXFVB matings. Genotyping was done by PCR analysis of the DNA from tail biopsies using primers against specific sequences in the expression cassette. Expression levels of

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mIL-17E were determined by ~~Taqman~~ TAQMAN<sup>TM</sup> RT-PCR reactions (Perkin Elmer) on total RNA samples derived from muscle biopsy.

*Determination of gene expression*

Total RNA samples from various mouse tissues were prepared using ~~TRIZOL~~ TRIZOL<sup>TM</sup> Reagent according to manufacturer's instructions (GIBCO-BRL). The mRNA expression levels for various cytokines, chemokines and adhesion molecules and IL-17RH1 (IL-17E receptor) were determined by ~~Taqman~~ TAQMAN<sup>TM</sup> RT-PCR (Perkin-Elmer) using gene specific primers and probes. Expression levels of 18S gene were used as normalization control.